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REMARKS

Claims 1 and 13-14 are amended. Upon entry of this amendment, claims 1-14 are currently pending and under examination. Claims 7-9 have been withdrawn from consideration by the Examiner as being drawn to a non-elected invention. As discussed below, Applicants request that claims 7-9 be examined in this application. Claims 15-26 have previously been canceled. No new matter was added by this amendment. Entry of the amendment is respectfully requested.

The Interview

The Applicant gratefully acknowledges on the record that the Examiner kindly granted a telephonic interview on Monday, January 22, 2007 at 4:30 PM EST. Present at this telephonic interview were Dr. Michael R. Ward, Attorney for Applicant; Dr. Marc K. Hellerstein (the inventor); and Dr. Irvin J. Mettler representing the University of California (the assignee). During the interview, Dr. Marc K. Hellerstein explained the invention and how it differs from Nanjee *et al. (infra)*. This response is submitted pursuant to those discussions.

The Amendment

The claims have been amended to expedite prosecution and advance the case toward allowance.

Claim 1 has been amended for further clarification. Steps a) – c) have been re-worded for claritiy. Step d) now indicates that the rate of dilution of the isotopically labeled cholesterol molecules is by endogenous unlabeled cholesterol to determine the rate of the first arm of reverse cholesterol transport in the living system. Thus, *dilution by unlabeled cholesterol* allows for the determination of the first arm of cholesterol synthesis. Support for this amendment can be found, for example, in paragraphs [0012] and [0050] (see US 2005/0249664A1, *i.e.*, the publication of the present application).

Election

The Examiner has made the restriction requirement final. Applicants reiterate that at least step d) ("calculating the rate of dilution... to determine the rate of the first arm of reverse

cholesterol transport in the living system") which is present in independent claim 1, claims 2-14 (which depend from claim 1), and in each of the inventions of Groups I-VI, is a special technical feature that "define[s] a contribution, which each of the inventions, considered as a whole, makes over the prior art." PCT Rule 13.2. As discussed in the response to the restriction requirement, Scheibner *et al.* does not disclose this key technical feature. As explained below, Nanjee *et al.* (*infra*) also fails to disclose this feature. Thus, the traversal of the restriction is respectfully reiterated.

Applicants respectfully request that the Examiner examine claims 7-9 (which depend form claims 1) at this time.

Specification

The Examiner indicates that the abstract needs correction because it must be in form of a single paragraph, and thus, a new abstract on a separate page is required.

The publication of this application, *i.e.*, US 2005/0249664A1 depicts the abstract as a single paragraph. Review of the application via private PAIR shows that the abstract appears on a single page as a single paragraph. Thus, it appears that a correction of the abstract should no longer be required. If the Examiner believes that a correction is still required, Applicant respectfully requests clarification.

Rejection Under 35 U.S.C. §102

Claims 1, 10, 12-14 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Nanjee *et al.* (Journal of *Lipid Res.* 2001; 42:1586-1593). The Office Action indicates:

> Nanjee et al. teach a method for determining the rate of cholesterol transport in humans with isotopically labeled cholesterol via intravenous infusion (page 1587, left column, 3rd full paragraph), obtaining labeled cholesterol from blood (where plasma HDL is obtained) (page 1587, right column, 3rd paragraph), measuring and calculating the rate of change of isotopic content (page 1588, left column, 3rd paragraph) by liquid scintillation spectrometer (page 1588, left column, end of 2nd full paragraph).

The rejection is respectfully traversed.

In order for a rejection under §102(b) to be valid, each and every element of the claim must be found in the prior art reference.[1]

The claims refer to a method that determines the rate of the first arm of reverse cholesterol transport through calculation of the *rate of dilution* of labeled cholesterol molecules **by endogenous unlabeled cholesterol** (see step d)). As supported in the specificaton, "[t]he present invention provides methods for determining reverse cholesterol transport (RCT) *in vivo* by measuring the flow of unlabeled cholesterol from tissues into the bloodstream and/or from plasma HDL to bile acids, instead of the flow of labeled cholesterol." See paragraph [0047]. This has the advantage that a quantitative value can be obtained in a relatively short period of time, providing for an accurate measurement of the first arm of RCT.

In contrast, Nanjee *et al.* (herein "Nanjee") do not measure the flow of endogenous unlabeled cholesterol nor do they calculate the rate of dilution of labeled cholesterol. In fact, **Nanjee disclose nothing about calculating the rate of dilution by endogenous unlabeled cholesterol**. Rather, Nanjee measure the flow of labeled cholesterol (*i.e.*, exogenous labeled cholesterol) from tissue to stool by administering labeled cholesterol, waiting for two to three months, measuring plasma-specific radioactivity to ensure that the label has washed out of the plasma, and then measuring incorporation of the label into the stool (see *Clinical Procedures* on page 1587, columns 1 and 2). As such, Nanjee cannot achieve an accurate quantitative rate measurement but merely a qualitative one, *i.e.*, any given measured concentration of labeled cholesterol may be higher or lower but no actual rate value or number can be obtained. Notably, it is not possible to calculate the rate of dilution of labeled cholesterol by endogenous unlabeled cholesterol by measuring plasma-specific radioactivity two to three months after administration of labeled cholesterol. Consequently, Nanjee cannot anticipate the present claims.

In view of the above amendments and remarks, Applicant respectfully requests withdrawal of the rejection.

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[1] See MPEP 2131; *In re Royka and Martin*, 180 USPQ 580 (CCPA 1974).

Rejection Under 35 U.S.C. §103

Claims 1-6 and 10-14 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Nanjee *et al.* in view of Hulzebos *et al.* (Journal of *Lipid Res.* 2001; 42:1923-1929).

The rejection is respectfully traversed.

All limitation of the claims must be suggested by the combination of references cited as prior art in order to establish *prima facie* obviousness.[2]

As discussed above, Nanjee disclose nothing about calculating the rate of dilution of endogenous unlabeled cholesterol. Nanjee measure only the flow of exogenous labeled cholesterol. Similarly, Hulzebos *et al.* (herein "Hulzebos") is directed to administration of labeled cholic acid and again, teaches nothing about calculating the rate of dilution by endogenous unlabeled cholesterol. See *Materials and Methods* on page 1924, column 1. As such, the combined references fail to teach or even suggest all of the elements of the claimed invention. Hence, the present claims cannot be obvious in light of Nanjee and Hulzebos. Consequently, the Examiner has failed to established a proper *prima facie* case of obviousness.

In view of the above amendments and remarks, Applicant respectfully requests withdrawal of the rejection.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and

[2] MPEP 2143.03; *In re Royka and Martin*, 180 USPQ 580 (CCPA 1974).

authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **416272003900**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: February 8, 2007

Respectfully submitted,

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